(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
5 June 2003 (05.06.2003)

PCT

(10) International Publication Number
WO 2003/045128 A3

(51) International Patent Classification[7]: A61K 38/16

(21) International Application Number:
PCT/US2002/037634

(22) International Filing Date:
21 November 2002 (21.11.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/331,801 21 November 2001 (21.11.2001) US

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(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*
— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

(88) Date of publication of the international search report:
6 April 2006

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 2003/045128 A3

(54) Title: SYNTHETIC IMMUNOGENIC BUT NON-DEPOSIT-FORMING POLYPEPTIDES AND PEPTIDES HOMOLOGOUS TO AMYLOID β, PRION PROTEIN, AMYLIN, α-SYNUCLEIN, OR POLYGLUTAMINE REPEATS FOR INDUCTION OF AN IMMUNE RESPONSE THERETO

(57) Abstract: The present invention relates to immunogenic but non-depositing-forming polypeptides or peptides homologous to amyloid β, prion, amylin or α-synuclein which can be used alone or conjugated to an immunostimulatory molecule in an immunizing composition for inducing an immune response to amyloid β peptides and amyloid deposits, to prion protein and prion deposits, to amylin and amylin deposits, to α-synuclein and deposits containing α-synuclein, or to polyglutamine repeats and deposits of proteins containing polyglutamine repeats. Described are also antibodies directed against such peptides, their generation, and their use in methods of passive immunization to such peptides and deposits.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US02/37634

A. CLASSIFICATION OF SUBJECT MATTER
IPC(7) : A61K 38/16
US CL : 514/12
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 514/12

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EAST, Pubmed

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	SIGURDSSON et al. Immunization with a notoxic/nonfibrillar amyloid-beta homologous peptide reduces Alzheimer's disease-associated pathology in transgenic mice. American Journal of Pathology. August 2001, Vol. 159, No. 2, pages 439-447. See page 440, first column.	1-2,8,16-20
Y	PODUSLO et al. Beth-Sheet Breaker Peptide Inhibitor of Alzheimer's Amyloidogenesis with Increased Blood-Brain Barrier Permeability and Resistance to Proteolytic Degradation in Plasma. J. Neurobiol. 1999, See page 375, second column, first complete paragraph.	1-2,4,5,9,10,11,13,14,16-20
Y	SIGURDSSON et al. In Vivo Reversal of Amyloid-Beth Lesions in Rat Brain Journal of Neuropathology and Experimental Neurology. January 2000, Vol. 59, No. 2, pages :11-17. See p. 11, second paragraph	16
Y	LOWENADLER et al. Enhanced Immunogenicity of Recombinant Peptide fusions Containing Multiple Copies of a Heterologous T. Helper Epitope. European Journal of Immunology. 1990. Vol. 20, pages 1541-1545, see entire document.	17-20
Y	WOOD et al Prolines and Amyloidogenicity in Fragments of the Alzheimer's Peptide Beth/A4. Biochemistry. 1995, Vol. 34, pages 724-730. See page 726, Table 1.	1-2,11

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search
10 November 2005 (10.11.2005)

Date of mailing of the international search report
07 FEB 2006

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Form PCT/ISA/210 (second sheet) (July 1998)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US02/37634

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claim Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-20

Remark on Protest
☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

PCT/US02/37634

INTERNATIONAL SEARCH REPORT

C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,E --- Y,E	US 6,713,450 B2 (FRANGIONE et al.) 30 March 2004(30.03.2004) See column 6 lines 22 - 46, SEQ ID NO:2,3, 12, column 8 lines 42-67, column 9 lines 45-65.	1-3,6-8,12,13,15-20 --- 4,5, 9,10,11,14

INTERNATIONAL SEARCH REPORT

PCT/US02/37634

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group 1, claim(s) 1 - 20, drawn to isolated polypeptides, polypeptides cross-linked to polymers, immunizing compositions, and methods of inducing immune responses, wherein the polypeptides have the sequence identified by the formula in claim 1.

Group 2, claim(s) 21, drawn to a method of reducing amyloidosis by administering polypeptides with the sequence identified by the formula in claim 1.

Group 3, claim(s) 22 - 26, drawn to molecules comprising antigen-binding regions of antibodies raised against polypeptides that have the sequence identified by the formula in claim 1, pharmaceutical compositions comprising same, methods of reducing the formation of amyloid fibrils and amyloidosis.

Group 4, claim(s) 27 - 44, drawn to isolated polypeptides, polypeptides cross-linked to polymers, immunizing compositions, and methods of inducing immune responses, wherein the polypeptides have the sequence identified by the formula in claim 27.

Group 5, claim(s) 45 - 48, drawn to molecules comprising antigen-binding regions of antibodies raised against polypeptides that have the sequence identified by the formula in claim 27, pharmaceutical compositions, and methods of reducing the formation of abnormal PrP^{sc} for of prion protein.

Group 6, claim(s) 49 - 65, drawn to isolated polypeptides as defined in claim 49, polypeptides conjugated to polymers, immunizing compositions, and methods of inducing immune responses to prion protein and prion deposits.

Group 7, claim(s) 66 - 69, drawn to molecules comprising antigen-binding regions of antibodies raised against polypeptides as defined in claim 49, pharmaceutical compositions comprising same, and methods of reducing the formation of abnormal form of prion protein in a cow.

Group 8, claim(s) 70 - 82, drawn to isolated polypeptides defined in claim 70, polypeptides conjugated to polymers, immunizing compositions, and methods of inducing immune responses.

Group 9, claim(s) 83, drawn to a method of reducing amyloidosis.

Group 10, claim(s) 84 - 87, drawn to molecules comprising antigen-binding regions of antibodies raised against polypeptides as defined in claim 70, pharmaceutical compositions comprising same, and methods of reducing amylin fibril formation.

Group 11, claim(s) 88, drawn to a method of reducing amyloidosis.

Group 12, claim(s) 89 - 97, drawn to isolated polypeptides defined in claim 89, polypeptides conjugated to polymers, immunizing compositions, and methods of inducing immune responses.

Group 13, claim(s) 98, drawn to a method of reducing amyloidosis.

Group 14, claim(s) 99 - 102, drawn to molecules comprising antigen-binding regions of antibodies raised against polypeptides as defined in claim 89, pharmaceutical compositions comprising same, and methods of reducing Lewy body formation.

Group 15, claim(s) 103, drawn to a method of reducing amyloidosis.

Group 16, claim(s) 104 - 109, drawn to isolated polypeptides defined in claim 104, polypeptides conjugated to polymers, immunizing compositions, and methods of inducing immune responses.

Group 17, claim(s) 110, drawn to a method of reducing amyloidosis.

Group 18, claim(s) 111 - 114, drawn to molecules comprising antigen-binding regions of antibodies raised against polypeptides as defined in claim 104, pharmaceutical compositions comprising same, and methods of reducing formation of protein aggegates.

Group 19, claim(s) 115, drawn to a method of reducing amyloidosis.

The inventions listed as Groups 1 - 19 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: the first stated technical feature is the isolated polypeptides set forth in claim 1. Group 1 includes those polypeptides, said polypeptides conjugated to polymers, immunizing compositions, and the first stated method of using the polypeptides. Applicant has not claimed a method of making the polypeptides. Group 2 is drawn to different methods of using the products. Groups 3 - 19 are drawn to different products (e.g. molecules comprising antigen binding regions of antibodies and different polypeptides with distinct core sequences) and to methods of using those other products. The different products do not share a common technical feature with the polypeptides of group 1; the methods of using those products also do not share a common technical feature with the polypeptides of group 1. Therefore there is not a special technical feature which links all inventions.